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SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/244,530	08/02/94	COLPAN	M P965024298

EXAMINER	
CRANE, L	
ART UNIT	**PAPER NUMBER**
1803	10

18M2/0531

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DATE MAILED: 05/31/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 03/17/95 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), ~~-------~~ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1-33 and 35-39 ---------- are pending in the application.
   Of the above, claims 17-31, 36 and 38-39 ---------- are withdrawn from consideration.
2. ☒ Claims 34 ---------- has ~~have~~ been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-16, 32-33, 35 and 37 ---------- are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).
12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____.
13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group 1800, Art Unit 1803.

Claim **34** has been cancelled.

Claims **1-33 and 35-38** remain in the case.

Applicant's election of Group I, claims **1-17, 32-33, 35 and 37** in Paper No. **9** is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a)).

Claims **17-31, 36 and 38** are withdrawn from further consideration by the examiner, 37 C.F.R. §1.142(b), as being drawn to a non-elected invention. Claim **39** is deemed to be a separate invention in view of terminology directed to the improvement of an enzymatic process and is this properly a replacement of cancelled claim **34**, the sole claim in Group **III**. Election was made **without** traverse in Paper No. **9**.

Applicant is requested to note that claims **12-15 and 32-33** violate both 35 U.S.C. §101 and 35 U.S.C. §112 since they are each drafted in terms of "use." See *Clinical Products v. Brenner*, 255 F. Supp. 151, 149 USPQ 475 (1966). In claims **12-13** the term "employed" is deemed to be the equivalent of the term "use".

Claim **33** is objected to under 37 C.F..R §1.75(c) as being in improper form because a multiple dependent claim must be drafted in

proper alternative form. See MPEP 603.01(i).

Claims **1-16, 32-33, 35 and 37** are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims **1, 35 and 37** applicant has claimed a process without using standard --comprising-- language. This is deemed to be an error of omission which leads to difficulties with dependent claims which contain a similar error in that they fail to use the term --further comprising-- when adding to the subject matter included within the independent claim, e.g. claim **3**. In these claims this language means that the claimed subject matter may not be viewed as including any other subject matter, i.e. in the absence of open language, closed language is assumed.

In claim **1** at line 3 of part "c)", the term "and/or" is deemed to be indefinite because it is unclear what applicant has claimed in the entirety of section c) due in part to the presence of the instant term. For example, is applicant claiming the adsorption of nucleic acids from solutions containing high ionic strength buffers alone, or these buffers plus an alcohol, or plus polyethylene glycol, or plus both an alcohol and polyethylene glycol or all four possibilities or some selected subset? Applicant is requested to consider using Markush terminology (selected from the group consisting of) in addressing this rejection.

In claim **3**, the addition of a centrifugation or filtration step prior to step "a)" is improper for lack of adequate antecedent basis in claim **1**. This problem may be overcome by proper introduction of

--comprising-- language in claim **1** and --further comprising-- language in the instant claim. This claim is also confusing because it appears to require the repetition of a step already in subsection a) of claim **1**, namely the process whereby "cell debris is removed."

In claims **9, 11, 12 and 13** applicant is requested to consider using Markush language (selected from the group consisting of) to introduce the various nucleic acids or mineral supports being claimed.

In claims **32-33** the term "use" is indefinite for failure to specify which step or steps are being referred to in the independent claim, i.e. which step uses which buffer? or which concentrations or which buffer? etc.

The following is a quotation of 35 U.S.C. §103 which forms the basis for all obviousness rejections set forth in this Office action:

> "A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person."

Claims **1-16 and 32-33** are rejected under 35 U.S.C. §103 as

being unpatentable over Hagen et al. '381 in combination with Sternberg '142 and further in view of Henco et al. '426, Riesner et al. '717 and Little '430.

The instant claims are directed to a process for DNA purification with the following steps: i) cell lysis and debris removal; ii) contacting with anion exchange resin in buffers of low ionic strength; iii) elution of the DNA from the resin by contacting the resin with high ionic strength buffer, iv) following the optional addition of a lower alcohol, or the further optional addition of polyethylene glycol, contacting the eluate with a mineral support material to effect adsorption of the DNA onto the mineral support material, and v) elution of DNA from the support material by contacting the mineral support material with a low ionic strength buffer or with water.

Hagen et al. '381 at column 8, lines 22-31, discloses the stacking of sheets of filtration materials.

Sternberg '142 at column 6, line 9, discloses variation in the porosity of multiple membrane discs usable in the described filtration apparatus and, at line 60, also teaches the application of "ion exchange sheet separation techniques" in concert with the claimed invention.

Henco et al. '426 at column 12, lines 23-25 discloses the use of "narrowpore sterile filters ... to retain intact cells or floating cell debris" as part of a DNA separation protocol which subsequently used the variation of ionic strength to separate DNA using an anion exchange resin. Henco also discloses the use of centrifugation in column 112 (see example 1), and subsequently also notes the utility of polyethylene glycol and isopropanol to induce the precipitation of DNA

at column 12, lines 41-44.

Riesner et al. '717 discloses at column 5, lines 21-59, the preparation of weak anion exchange resins and subsequently at column 6, lines 31-40 how said resin was used to effect the chromatographic purification of DNA.

Little '430 at column 7, lines 12-45, discloses one of several examples wherein DNA is extracted from cells of various types using chaotropic ion/enzyme-mediated digestion followed by centrifugation and ultimately chromatographic separation using a commercial diatomaceous earth (Celite) and various buffer solutions.

Applicant's combination of conventional physical separation of cell debris, followed by anionic exchange chromatography and ultimately by mineral support chromatography to effect the purification of DNA is a combination of process steps well known in the prior art and motivated by the disclosures of Henco et al. '426, Riesner et al. '717 and Little '430. The use of a specific filtration methodology (i.e. variation in filter porosity) such as those taught by Hagen et al. '381 or Sternberg '142 is deemed to be incorporation of a variation clearly within the perview of the ordinary practitioner seeking to optimize the result of the Henco methodology. Thus, applicants specific process is deemed to have been subject matter clearly within the perview of the ordinary practitioner at the time of the instant filing date and that the results obtained herein were available to the ordinary practitioner at that time by merely combining the processes of the prior art. Therefore, said subject matter is found to include no adequate basis for a finding of patentability in view of the noted prior art.

Therefore, the instant claims would have been obvious to one of ordinary skill in the art having the above cited references before him at the time the invention was made.

Claim **35** is rejected under 35 U.S.C. §103 as being unpatentable over Hagen et al. '381 in combination with Schneider '080 and Sternberg '142 and further in view of Henco et al. '426 or Riesner et al. '717.

The instant claim is directed to a process of nucleic acid purification wherein the first step is a filtration step and the second step contacts the effluent from the first step with an anionic exchange resin.

Hagen et al. '381 at column 8, lines 22-31, discloses the stacking of sheets of filtration materials.

Schneider '080 at columns 2-3 discloses the separation of nucleic acid adsorbed on an anion exchange resin by filtration.

Sternberg '142 at column 6, line 9, discloses variation in the porosity of multiple membrane discs usable in the described filtration apparatus and, at line 60, also teaches the application of "ion exchange sheet separation techniques" in concert with the claimed invention.

Henco et al. '426 at column 12, lines 23-25 discloses the use of "narrowpore sterile filters ... to retain intact cells or floating cell debris" as part of a DNA separation protocol which subsequently used the variation of ionic strength to separate DNA using an anion exchange resin.

Riesner et al. '717 discloses at column 5, lines 21-59, the preparation of weak anion exchange resins and subsequently at column 6, lines 31-40 how said resin was used to effect the chromatographic purification of DNA.

Applicant's combination of variable porosity filtration and anionic exchange chromatography to effect the purification of DNA is a combination of process steps well known in the prior art and motivated by the disclosures of Henco et al. '426 and secondarily by the disclosures of Riesner and Schneider. The use of a specific filtration methodology (i.e. variation in filter porosity) such as those disclosed by Hagen et al. '381 or Sternberg '142 is deemed to be incorporation of a variation clearly within the perview of the ordinary practitioner seeking to optimize the result of the Henco methodology. Thus, applicants specific process is deemed to have been subject matter clearly within the perview of the ordinary practitioner at the time of the instant filing date. Therefore, said subject matter is found to include no adequate basis for a finding of patentability in view of the noted prior art.

Therefore, the instant claims would have been obvious to one of ordinary skill in the art having the above cited references before him at the time the invention was made.

Claim **37** is rejected under 35 U.S.C. §103 as being unpatentable over Hagen et al. '381 in combination with Sternberg '142 and further in view of Henco et al. '426 in combination with Little '430.

The instant claim is directed to a process of nucleic acid purification wherein the first step is a filtration step and the second

step contacts the effluent from the first step with an anionic exchange resin.

The relevant disclosures in Hagen et al. '381 and Sternberg '142 are described above.

Henco et al. '426 at column 12, lines 23-25 discloses the use of "narrowpore sterile filters ... to retain intact cells or floating cell debris" as part of a DNA separation protocol which subsequently used the variation of ionic strength to separate DNA using an anion exchange resin. Henco et al. '426 at column 11, lines 53-59, also discloses the use of centrifugation as a preliminary purification procedure in DNA purification, but Henco does not disclose the use of a mineral adsorbant for chromatographic purification of DNA.

Little '430 at column 7, lines 12-45, discloses one of several examples wherein DNA is extracted from cells of various types using chaotropic ion/enzyme-mediated digestion followed by centrifugation and ultimately chromatographic separation using a commercial diatomaceous earth (Celite) and various buffer solutions.

Applicant's combination of the steps of variable porosity filtration and "mineral support" chromatography to effect the purification of DNA is a combination of process steps well known in the prior art and motivated by the disclosures of Henco et al. '426 and Little '430 in combination. The use of a specific filtration methodology (i.e. variation in filter porosity) such as those disclosed by Hagen et al. '381 or Sternberg '142 is deemed to be incorporation of a variation clearly within the perview of the ordinary practitioner seeking to optimize the result of the Henco/Little methodologies. Thus, applicants specific process is deemed to have been subject matter

clearly within the perview of the ordinary practitioner at the time of the instant filing date. Therefore, said subject matter is found to include no adequate basis for a finding of patentability in view of the noted prior art.

Therefore, the instant claims would have been obvious to one of ordinary skill in the art having the above cited references before him at the time the invention was made.

The remaining art made of record in some cases duplicates the subject matter of the art cited in the rejections supra and has been included for the sake of completeness. Remaining art not cited above is deemed to be closely related and has been cited only to show the state of the art.

Papers related to this application may be submitted to Group 1800 via facsimile transmission(FAX). The transmission of such papers must conform with the notice published in the Official Gazette (1096 OG 30, November 15, 1989). The telephone number for the FAX machine now on-line in Group Art Unit 1803 is (703) **308-4227** .

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner L. E. Crane whose telephone number is 703-**308-4639** . The examiner can normally be reached between 9:30 AM and 5:00 PM, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Douglas W. Robinson, can be reached on (703)-308-2897.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1800 receptionist whose telephone number is 703-**308-0196** .

LECrane:lec

5 5/29/95

DOUGLAS W. ROBINSON
SUPERVISORY PATENT EXAMINER
GROUP 1800